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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/762,588
Filing Date: 02/06/2007
Appellant(s): TCHAGA et al.

Bret Field
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 02/06/2007 appealing from the Office action mailed on 11/27/2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

Examiner is not aware of any related proceedings.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

The appeal involves claims 11-13, 16, 18-21, 23 and 24 that are pending and all of which are rejected. Claims 11-13, 16, 18-21, 23 and 24 are appealed.

(4) Status of Amendments After Final

There are no pending amendments.

(5) Summary of Claimed Subject Matter

The summary of invention contained in the brief is correct.

(6) Grounds of Rejection to be reviewed on Appeal

The Appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

1. Tchaga et al. (WO 99/57992).

2. Porath et al. (Biochemistry, 1983: 22; p. 1621-1630).

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

The rejection of claims 11-13, 16, 18-21, and 23-24 under 35 U.S.C. 103(a) as being unpatentable over Tchaga et al. (WO 99/57992) in view of Porath et al. (Biochemistry, 1983: 22; p. 1621-1630).

Claims 11-13, 16, 18-21, and 23-24 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Tchaga et al. (WO 99/57992) in view of by Porath et al.("Immobilized Metal Ion Affinity Adsorption and Immobilized Metal Ion Affinity Chromatography of Biomaterials. Serum Protein Affinities for Gel-Immobilized Iron and Nickel Ions," Biochemistry (1983), 22, p. 1621-1630).

Tchaga et al. teach the instant SEQ ID NO:1 in the sequence listing section on page SEQ 7/7, as SEQ ID NO:6, which is a metal affinity peptide.

In Tchaga et al., Figures 1, 2, and 3 depict different vectors comprising, for example, SEQ ID NO:6 with different restriction sites, and on pages 19 and 20 of the specification, the invention teaches recombinant vector comprising DNA sequence where the recombinant vector is capable of directing expression of said DNA sequence for the fusion protein. See also pages 22 and 23, for claims 1, 2, 6-9 of Tchaga et al.

Also, on page 9 lines 21-24 of the specification, metals that can be used for purification or immobilization of fusion proteins are disclosed and include, Ni(II), Co(II), Zn(II), Cu(II), Ac(III) and Fe(III).

Further, Tchaga et al. teach different buffers that can be used in the purification of proteins, see Example 4, pages 14 and 15.

Tchaga et al. do not teach two different columns/resins that are used in the purification.

Porath et al. teach metal chelate affinity chromatography for purification of serum proteins, where gels are loaded with the same or different metal ion, for example Ni(II) and Fe(III). See *Abstract*.

Porath et al. prepared different columns, for example "IDA-Sepharose 6B" or "TED-Sepharose 4 B" with bound Ni(II) or bound Fe(III), where each chelator gel was packed in a separate column. See page 1622 (*Materials and Methods* section).

Porath et al. teach different combinations of columns, where two or more columns were packed with one type of chelator gel (e.g., TED-Sepharose) and loaded with different metal ions (e.g., Ni(II) or Fe(III)) to form "tandem columns". See page 1622 (*Chromatography* section).

Further, different combinations of "tandem columns" were created where Fe(III)-TED bed proceeded Ni(II)-TED or Ni(II)-TED bed preceded Fe(III)-TED bed. See page1624 (*Results* section).

In addition, the following buffers were used for extraction, wash, and elution purposes: 0.05M sodium acetate and 0.1 M NaCl, pH 5.5; 0.1 M Tris-HCl, pH 8.1; 0.5 M sodium acetate, pH 5.5; and 1M glycine, pH 9.0 (claims 11 and 16).

It would have been obvious to one skilled in the art at the time the invention was made to use two different resins in combination, as taught by Porath et al., and include in the design a vector as taught by Tchaga et al. because these kind of designs of columns for purification of proteins are known and commonly used in the art. One would have been motivated to use the tandem column system used by Porath et al. because of its high efficiency of purification.

(10) Response to Argument:

Claims 11-13, 16, 18021 and 23-24 are obvious under 35 U.S.C. 103(a) over Tchaga et al. (WO 99/57992) in view of Porath et al. (Biochemistry, 1983; 22; p. 1621-1630).

Appellants in their Appeal Brief, on pages 5-7, divided the rejected claims into 6 Groups: Group I, claims 11, 16, and 23; Group II, claim 12; Group III, claim 13; Group IV, claims 18, 21, and 24; Group V, claim 19; and Group VI, claim 20.

However, for purposes of clarity and because the same issues and the same arguments are being presented for each of those 6 groups, Examiner responds to the Appellants' arguments in two groupings: a set of claims 11-13, 16, and 23 and another set of claims 18-21 and 24. The reason Examiner decided to respond to the Appellants' argument in this fashion is because the are only two independent claims: 11 and 18, and dependent claims 12, 13, 16, and 23 depend from claim 11, and dependent claims 19-21 and 24 depend from claim 18.

Thus, claims 11-13, 16 and 23 should be addressed together, and claim 18-21 and 24 should be addressed together since the same arguments are presented for each set of the claims.

Examiner addressing currently rejected claims 11-13, 16 and 23

First, Appellants state that there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the references teachings of Tchaga et al. and Porath et al. Further, Appellants assert that Tchaga et al. is directed to purification of a protein of interest

using ion affinity tags, which constitute short polypeptide sequences that are designed to complex metal ions with much higher efficiency than the attached native polypeptide. Next, Appellants state that Porath et al. is directed to the purification of polypeptides to which no ion affinity tag has been fused, i.e. native, untagged protein, whereas the purification process taught by Porath et al. depends entirely upon the affinity of various features of the native polypeptide sequence itself. In conclusion, Appellants state that there is no motivation and no reason to expect successes in applying a strategy for purifying untagged proteins to a method teaching the use and optimization of ion binding tags.

In response, the Examiner notes that the rejected claims 11-13, 16, and 23 are unpatentable over Tcahaga et al. in view of Porath et al. because Tchaga et al. teach different vectors with different restriction sites where the vectors direct expression of DNA sequence for a desired fusion protein where the ion affinity peptide is fused to the polypeptide of interest and where the fusion protein can be immobilized and purified on resins that include Ni(II), Co(II), Zn(II), Cu(II), Ac(III) and Fe(III). Further, Porath et al. teach resins with Ni(II) and Fe(III).

Examiner responds that there is no teaching in Tchaga et al. or Porath et al. that the metal ion chelate resin will distinguish between native and tagged proteins, since even though polyhistidine tags bind strongly to divalent metal ion, particularly nickel, the metal ion chelate resin can also be used for natural proteins that have inherent affinity for divalent or trivalent cations, such as Ni(II) and Fe(III) as taught by Poarth. Thus, tagged and untagged proteins can be used for immobilization and purification with metal

ion chelate resins because of their structural affinity to the positively charged metal ion. Examiner wishes to stress that, Appellants' arguments to the contrary, both references deal directly with the same area of endeavor, that is, the art of protein purification, and the fact that Porath et al. take advantage of the properties that the protein to be purified already has and Tchaga et al. add the desired properties is no practical difference at all.

Second, Appellants assert that Tchaga et al. are silent with regard to the use of more than one column, where the references fail to teach or suggest all of the elements of claim 12, (see Applicant's arguments on page 13). Further, with regard to claim 13, Appellants state that Tchaga et al. is silent with regard to the use of more than one column, (see Appellants' remarks on page 14).

Examiner responds that claims 12 and 13 are unpatentable over Tchaga et al. in view of Porath et al. because Tchaga et al. teach different fusion proteins that are immobilized and purified utilizing metal ion chelate resin, where different cations: Ni(II), Co(II), Zn(II), Cu(II), Ac(III), and Fe(III) can be used, and Porath et al. teach that such chelate resins can be used in combination of two or three columns together in tandem. Therefore, the rejection is proper and there is a clear motivation to use two different resins with different metals of choice for immobilization or purification of different proteins of choice.

Examiner addressing currently rejected claims 18-21 and 24

Appellants state that Tchaga et al. are silent with regard to the use of more than one column and Porath et al. are silent with regard to a first composition including a first

metal ion chelate resin including immobilized Co(II) metal ion, and thus, Appellants assert, that there is no motivation to make the combination of teachings suggested by Examiner.

With regard to claim 19, Appellants state that Tchaga et al. are silent with regard to second column and about the identity of any second metal ion to be used in a second metal ion tandem column. Also, Appellants state that Porath et al. teach neither the use of Co(II) in an affinity column nor use of such a column in conjunction with a second column including an immobilized hard metal ion.

With regard to claim 20, Appellants state that Tchaga et al. are silent not only with regard to a second column, but also with regard to identity of any second metal ion to be used in a second, tandem column. Also, Appellants state that Tchaga et al. and Porath et al. are silent with regard to a first composition including a first metal ion chelate resin in which the first metal ion is Co(II) and second composition including a second metal ion chelate resin including a second immobilized hard metal ion chosen from Fe(III), Ca(II), and Al(III).

Examiner responds that claims 18-21 and 24 are unpatentable over Tchaga et al. in view of Porath et al. because Tchaga et al. teach the instant protein of SEQ ID NO:1, and also other fusion proteins that comprise a protein of interest fused at its amino-terminus or carboxy-terminus to at least one affinity peptide. Further, Tchaga et al. teach different metals that can be used for purification or immobilization of fusion proteins with resins, which include Ni(II), Co(II), Zn(II), Cu(II), Ac(III) and Fe(III).

Therefore, Tchaga et al. teach immobilization of fusion proteins, such as instant SEQ ID NO:1, and subsequently their purification using resins with metals, such as Co(II).

Additionally, Porath et al. teach two or more columns packed with a chelator gel and loaded with different metal ions, for example Ni(II) or Fe(III) to form tandem columns. Also, Porath et al. did not teach away that other metals, such as Co(II) would not work or be disadvantageous in the purification of proteins. Furthermore, using Co(II) as a choice of metal for chelate resins is an art-recognized equivalent as taught by Tchaga et al.

Therefore, the rejection is proper, since, as recognized by the prior art presented above, metal ions can be interchanged in a resin and different metal ions, such as Ni(II) or Fe(III) or Co(II) are widely used as recognized by Tchaga et al. Also, Porath et al. taught the different resins could be placed in two or three columns in a tandem formation for example. Thus, all limitations of the rejected claims are found in the prior art of record and the instant invention is obvious over Tchaga et al. in view of Porath et al. for the reasons aforementioned above.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the Examiner in the Related Appeals and Interferences section of this Examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Agnes B. Rooke

June 19, 2007

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